

**PATENT COOPERATION TREATY**  
**PCT**  
**INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY**  
(Chapter II of the Patent Cooperation Treaty)  
(PCT Article 36 and Rule 70)

Applicant's or agent's file reference <b>P-INCI-x-04-0277</b>	<b>FOR FURTHER ACTION</b>		See Form PCT/APEA/416
International application No. <b>PCT/EP2004/008514</b>	International filing date (day/month/year) <b>29.07.2004</b>	Priority date (day/month/year) <b>30.07.2003</b>	
<p>International Patent Classification (IPC) or national classification and IPC <b>A61K45/06, A61K31/00, A61P3/04, A61P3/10</b></p>			
<p>Applicant <b>LABORATORIOS DEL DR. ESTEVE S.A. et al.</b></p>			
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 5 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input checked="" type="checkbox"/> (<i>sent to the applicant and to the International Bureau</i>) a total of 26 sheets, as follows:</p> <ul style="list-style-type: none"> <li><input checked="" type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</li> <li><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</li> </ul> <p>b. <input type="checkbox"/> (<i>sent to the International Bureau only</i>) a total of (indicate type and number of electronic carrier(s)), containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>			
<p>4. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> <li><input checked="" type="checkbox"/> Box No. I Basis of the opinion</li> <li><input type="checkbox"/> Box No. II Priority</li> <li><input type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and Industrial applicability</li> <li><input type="checkbox"/> Box No. IV Lack of unity of invention</li> <li><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</li> <li><input type="checkbox"/> Box No. VI Certain documents cited</li> <li><input type="checkbox"/> Box No. VII Certain defects in the international application</li> <li><input type="checkbox"/> Box No. VIII Certain observations on the international application</li> </ul>			
Date of submission of the demand <b>28.02.2005</b>	Date of completion of this report <b>28.11.2005</b>		
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax +49 89 2399 - 4465	<p>Authorized Officer <b>Paul Soto, R</b></p> <p>Telephone No. +49 89 2399-7346</p> 		

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**INTERNATIONAL PRELIMINARY REPORT  
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**Box No. I Basis of the report**

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
  - This report is based on translations from the original language into the following language, which is the language of a translation furnished for the purposes of:
    - international search (under Rules 12.3 and 23.1(b))
    - publication of the international application (under Rule 12.4)
    - international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the elements\* of the international application, this report is based on (replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report):

**Description, Pages**

1-397 as originally filed

**Claims, Numbers**

1-41 received on 02.06.2005 with letter of 30.05.2005

- a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3.  The amendments have resulted in the cancellation of:
  - the description, pages
  - the claims, Nos. 42-45
  - the drawings, sheets/figs
  - the sequence listing (specify):
  - any table(s) related to sequence listing (specify):

4.  This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
  - the description, pages
  - the claims, Nos.
  - the drawings, sheets/figs
  - the sequence listing (specify):
  - any table(s) related to sequence listing (specify):

\* If item 4 applies, some or all of these sheets may be marked "superseded."

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**Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

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**1. Statement**

Novelty (N)	Yes:	Claims	1-41
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-41
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-41
	No:	Claims	

**2. Citations and explanations (Rule 70.7):****see separate sheet**

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**Re Item V**

**Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

**1. Reference is made to the following documents:**

- D1: WO 03/084952 A (ESTEVE LAB DR ESTEVE S A) 16 October 2003  
D2: WO 03/042175 A (ESTEVE LABOR DR) 22 May 2003  
D3: WO 03/039547 A (BIOVITRUM AB ; CALDIROLA PATRIZIA (SE)) 15 May 2003  
D4: WO 97/35881 A (NG GORDON Y K ; SEEMAN PHILIP (CA); DOWD BRIAN F O (CA); GEORGE SUSAN) 2 October 1997

If not indicated otherwise, the relevant passages are those mentioned in the International Search Report.

**2. The present application relates to:**

- (i) an active substance combination, characterised in that it comprises: (A) at least one compound with neuropeptide Y (NPY)-receptor affinity selected from the group consisting of the 1,4-disubstituted piperidine compounds of general formula (Ia), and (B) at least one compound with 5-HT<sub>6</sub> receptor affinity selected from the group consisting of the benzoxazinone-derived sulfonamide compounds of general formula (Ib), compounds derived from sulfonamide of general formula (Ic), compounds of general formula (Id), and compounds derived from sulfonamide of general formula (Ie), (If), (Ig), and (Ih) (**claim 1**);  
(ii) a medicament comprising said active substance combination (**claim 3**);  
(iii) the use of said combination for the manufacture of a medicament for regulation of appetite (**claim 5**), for maintenance, increase or reduction of body weight (**claim 6**); for prophylaxis and/or treatment of disorders related to food ingestion (**claim 7**) and for the therapeutic indications specified in **claims 8-29**;  
(iv) a pharmaceutical formulation, characterised in that it comprises said active substance combination (**claim 30**).

**3. The present application meets the requirements of the PCT with respect to novelty (Art. 33(2)) because none of the documents of the prior art discloses pharmaceutical**

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combinations comprising the two active compounds as specified in claim 1.

4. The present application does also meet the requirements of the PCT with respect to inventive step (Art. 33(3)).

The use of neuropeptide Y antagonists as therapeutic agents, and in particular for the control of appetite and the treatment/prevention of food ingestion related disorders is well known in the art (see for example D4). The present application according to claim 1 differs from D4 (which can be regarded as the closest prior art) in that the claimed pharmaceutical composition comprises specific Y antagonists, namely those of formula (Ia), and in that it further comprises compounds with 5-HT6 receptor affinity of the specified formulae (Ib), (Ic), (Id), (Ie), (If), (Ig), or (Ih).

Thus, the *problem* to be solved by the present application is the provision of alternative pharmaceutical compositions useful for the control of appetite and the treatment/prevention of food ingestion related disorders. The *solution* provided by the present application according to claim 1 involves an inventive step. Compounds with 5-HT6 receptor affinity are also well known in the art as therapeutic agents (see for example D3), and in particular also for the treatment of obesity, reduction of food intake, etc. Thus, it would be obvious for the skilled person to combine neuropeptide Y antagonists and compounds with 5-HT6 receptor affinity, since both are known to be useful for the treatment of these same therapeutic indications. However, the specific combination of neuropeptide Y antagonists of formula (Ia) and compounds with 5-HT6 receptor affinity of formulae (Ib)-(Ih) is not suggested or rendered somehow obvious by any prior art document.

5. Claims 1-41 meet the criterion set forth in Article 33(4) PCT because their subject-matter is susceptible of industrial application.

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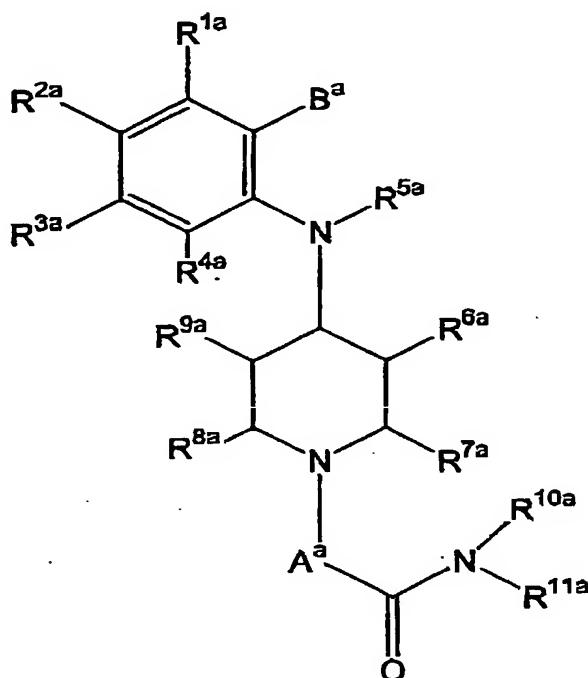
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## Amended Claims:

1. An active substance combination, characterized in that it comprises:

5 (A) at least one compound with neuropeptide Y (NPY) -receptor affinity selected from the group consisting of the 1,4-disubstituted piperidine compounds of general formula (la)



(la)

wherein

15  $R^{1a}$ ,  $R^{2a}$ ,  $R^{3a}$ ,  $R^{4a}$  are each independently selected from the group consisting of hydrogen, halogen, an unbranched or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic radical, a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing cycloaliphatic radical, which may be bonded via an optionally at least mono-substituted alkylene group and/or may be condensed with an optionally at least mono-substituted mono- or polycyclic ring-system, an optionally at least mono-substituted aryl- or heteroaryl radical,

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which may be bonded via an optionally at least mono-substituted alkylene group and/or may be condensed with an optionally at least mono-substituted mono- or polycyclic ringsystem, a nitro, cyano, -OR<sup>12a</sup>, -O-(C=O)R<sup>13a</sup>, -(C=O)-OR<sup>13a</sup>, -SR<sup>14a</sup>, -SOR<sup>14a</sup>, -SO<sub>2</sub>R<sup>14a</sup>, -NH-SO<sub>2</sub>R<sup>14a</sup>, -SO<sub>2</sub>NH<sub>2</sub> and -NR<sup>15a</sup>R<sup>16a</sup> moiety,

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R<sup>5a</sup> represents hydrogen, an unbranched or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic radical, or a saturated or unsaturated, optionally at least mono-substituted cycloaliphatic radical,

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R<sup>6a</sup>, R<sup>7a</sup>, R<sup>8a</sup>, R<sup>9a</sup> are each independently selected from the group consisting of hydrogen, an unbranched or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic radical, a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing cycloaliphatic radical, a cyano and a COOR<sup>17a</sup> moiety,

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A<sup>a</sup> represents a bridge member -CHR<sup>18a</sup>- or -CHR<sup>18a</sup>-CH<sub>2</sub>-,

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B<sup>a</sup> represents an unbranched or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic radical, a saturated or unsaturated, optionally at least mono-substituted cycloaliphatic radical, a COOR<sup>19a</sup>-moiety, a -(C=O)R<sup>20a</sup>-moiety, or a -CH<sub>2</sub>OR<sup>23a</sup>-moiety,

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R<sup>10a</sup> represents hydrogen, an unbranched or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic radical, a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing cycloaliphatic radical or an optionally at least mono-substituted aryl- or heteroaryl radical, which may be bonded via an optionally at least mono-substituted alkylene group and/or may be condensed with an optionally at least mono-substituted mono- or polycyclic ring-system,

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$R^{11a}$  represents an unbranched or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic radical, a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing cycloaliphatic radical, which may be bonded via an optionally at least mono-substituted alkylene group and/or may be condensed with an optionally at least mono-substituted mono- or polycyclic ringsystem, or an optionally at least mono substituted aryl- or heteroaryl radical, which may be bonded via an optionally at least mono-substituted alkylene group and/or may be condensed with an optionally at least mono-substituted mono- or polycyclic ringsystem, or

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$R^{10a}$  and  $R^{11a}$  together with the bridging nitrogen atom form an optionally at least mono-substituted, saturated, unsaturated or aromatic heterocyclic ring that may contain at least one further heteroatom as a ring member and/or may be condensed with an optionally at least mono-substituted mono- or polycyclic ringsystem,

20

25

$R^{12a}$  represents hydrogen, an unbranched or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic radical, a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing cycloaliphatic radical, which may be bonded via an optionally at least mono-substituted alkylene group and/or may be condensed with an optionally at least mono-substituted mono- or polycyclic ring-system, or an optionally at least mono-substituted aryl- or heteroaryl radical, which may be bonded via an optionally at least mono-substituted alkylene group and/or may be condensed with an optionally at least mono-substituted mono- or polycyclic ring-system,

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$R^{13a}$  represents hydrogen, an unbranched or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic radical, a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing cycloaliphatic radical, which may be bonded via an optionally at least mono-substituted alkylene group and/or may be condensed with an optionally at least mono-substituted mono- or polycyclic

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ring-system, or an optionally at least mono-substituted aryl- or heteroaryl radical, which may be bonded via an optionally at least mono-substituted alkylene group and/or may be condensed with an optionally at least mono-substituted mono- or polycyclic ring-system,

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$R^{14a}$  represents an unbranched or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic radical, a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing cycloaliphatic radical, which may be bonded via an optionally at least mono-substituted alkylene group and/or may be condensed with an optionally at least mono-substituted mono- or polycyclic ring-system, or an optionally at least mono-substituted aryl- or heteroaryl radical, which may be bonded via an optionally at least mono-substituted alkylene group and/or may be condensed with an optionally at least mono-substituted mono- or polycyclic ring-system,

10

$R^{15a}$  and  $R^{16a}$  each are independently selected from the group consisting of hydrogen, an unbranched or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic radical, a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing cycloaliphatic radical, which may be bonded via an optionally at least mono-substituted alkylene group and/or may be condensed with an optionally at least mono-substituted mono- or polycyclic ring-system, or an optionally at least mono-substituted aryl- or heteroaryl radical, which may be bonded via an optionally at least mono-substituted alkylene group and/or may be condensed with an optionally at least mono-substituted mono- or polycyclic ring-system,

20

or  $R^{15a}$  and  $R^{16a}$  together with the bridging nitrogen atom form a saturated, unsaturated or aromatic heterocyclic ring, which may be at least mono-substituted and/or contain at least one further heteroatom as a ring member,

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5      R<sup>17a</sup> represents hydrogen, an unbranched or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic radical, a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing cycloaliphatic radical or an optionally at least mono-substituted aryl- or heteroaryl radical, which may be bonded via an optionally at least mono-substituted alkylene group and/or may be condensed with an optionally at least mono-substituted mono- or polycyclic ring-system,

10     ○ R<sup>18a</sup> represents hydrogen, an unbranched or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic radical, a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing cycloaliphatic radical or an optionally at least mono-substituted aryl- or heteroaryl radical, which may be bonded via an optionally at least mono-substituted alkylene group and/or may be condensed with an optionally at least mono-substituted mono- or polycyclic ring-system,

15     ○ R<sup>19a</sup> represents hydrogen, an unbranched or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic radical, a saturated or unsaturated, optionally at least mono-substituted cycloaliphatic radical, or an optionally at least mono-substituted aryl- or heteroaryl radical, which may be condensed with an optionally at least mono-substituted mono- or polycyclic ring-system,

20     ○ R<sup>20a</sup> represents hydrogen, an unbranched or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic radical, a saturated or unsaturated, optionally at least mono-substituted cycloaliphatic radical, an optionally at least mono-substituted aryl- or heteroaryl radical, which may be condensed with an optionally at least mono-substituted mono- or polycyclic ring-system, or a NR<sup>21a</sup>R<sup>22a</sup>-moiety.

25     30 R<sup>21a</sup> represents hydrogen, an unbranched or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic radical, a saturated or unsaturated, optionally at least mono-substituted cycloaliphatic radical, or an optionally at least mono-substituted aryl- or heteroaryl radical, which may

be condensed with an optionally at least mono-substituted mono- or polycyclic ring-system,

5      R<sup>22a</sup> represents hydrogen, an unbranched or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic radical, a saturated or unsaturated, optionally at least mono-substituted cycloaliphatic radical, or an optionally at least mono-substituted aryl- or heteroaryl radical, which may be condensed with an optionally at least mono-substituted mono- or polycyclic ring-system,

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R<sup>23a</sup> represents hydrogen, an unbranched or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic radical, which may comprise at least one heteroatom as a chain member, or a -(C=O)R<sup>13a</sup>- moiety,

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optionally in form of one of its stereoisomers, preferably enantiomers or diastereomers, its racemate or in form of a mixture of at least two of its stereoisomers, preferably enantiomers or diastereomers, in any mixing ratio, or salts, preferably physiologically acceptable salts thereof, or corresponding solvates;

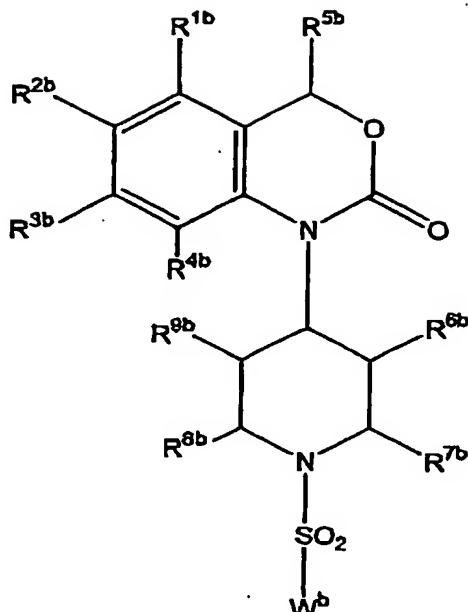
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and

(B) at least one compound with 5-HT<sub>6</sub> receptor affinity selected from the group consisting of the benzoxazinone-derived sulfonamide compounds of general formula (Ib)

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(lb)

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wherein

R<sup>1b</sup>, R<sup>2b</sup>, R<sup>3b</sup>, R<sup>4b</sup> are each independently selected from the group consisting of hydrogen, halogen, an unbranched or branched, saturated or unsaturated, 10 optionally at least mono-substituted aliphatic radical, a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing cycloaliphatic radical, which may be bonded via an optionally at least mono-substituted alkylene group and/or may be condensed with an optionally at least mono-substituted mono- or polycyclic ring-system, an optionally at least mono-substituted aryl- or heteroaryl radical, which may be bonded via an optionally at least mono-substituted alkylene group and/or may be condensed with an optionally at least mono-substituted 15 mono- or polycyclic ringsystem, a nitro, cyano, -OR<sup>10b</sup>, -O(C=O)R<sup>11b</sup>, -(C=O)OR<sup>11b</sup>, -SR<sup>12b</sup>, -SOR<sup>12b</sup>, -SO<sub>2</sub>R<sup>12b</sup>, -NH-SO<sub>2</sub>R<sup>12b</sup>, -SO<sub>2</sub>NH<sub>2</sub> and a -NR<sup>13b</sup>R<sup>14b</sup> moiety,

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R<sup>5b</sup> represents hydrogen, an unbranched or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic radical or a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing cycloaliphatic radical.

5 R<sup>6b</sup>, R<sup>7b</sup>, R<sup>8b</sup>, R<sup>9b</sup> are each independently selected from the group consisting of hydrogen, an unbranched or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic radical, a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing cycloaliphatic radical, a cyano group and a COOR<sup>15b</sup> moiety,

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W<sup>b</sup> represents an unbranched or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic radical,

15 a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing cycloaliphatic radical, which may be bonded via an optionally mono-substituted alkylene group and/or may be condensed with an optionally at least mono-substituted mono- or polycyclic ring-system.

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an optionally at least mono-substituted aryl or heteroaryl radical, which may be bonded via an optionally at least mono-substituted alkylene or alkenylene group and/or may be condensed with an optionally at least mono-substituted mono- or polycyclic ring-system,

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a NR<sup>16b</sup>R<sup>17b</sup>-moiety, or

a COR<sup>18b</sup>-moiety,

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R<sup>10b</sup> represents hydrogen, an unbranched or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic radical, a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing cycloaliphatic radical, which may be bonded via an optionally at least mono-substituted alkylene group and/or may

be condensed with an optionally at least mono-substituted mono- or polycyclic ring-system, or an optionally at least mono-substituted aryl- or heteroaryl radical, which may be bonded via an optionally at least mono-substituted alkylene group and/or may be condensed with an optionally at least mono-substituted mono- or polycyclic ring-system,

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$R^{11b}$  represents hydrogen, an unbranched or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic radical, a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing cycloaliphatic radical, which may be bonded via an optionally at least mono-substituted alkylene group and/or may be condensed with an optionally at least mono-substituted mono- or polycyclic ring-system, or an optionally at least mono-substituted aryl- or heteroaryl radical, which may be bonded via an optionally at least mono-substituted alkylene group and/or may be condensed with an optionally at least mono-substituted mono- or polycyclic ring-system,

$R^{12b}$  represents an unbranched or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic radical, a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing cycloaliphatic radical, which may be bonded via an optionally at least mono-substituted alkylene group and/or may be condensed with an optionally at least mono-substituted mono- or polycyclic ring-system, or an optionally at least mono-substituted aryl- or heteroaryl radical, which may be bonded via an optionally at least mono-substituted alkylene group and/or may be condensed with an optionally at least mono-substituted mono- or polycyclic ring-system,

$R^{13b}$  and  $R^{14b}$  each are independently selected from the group consisting of hydrogen, an unbranched or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic radical, a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing cycloaliphatic radical, which may be bonded via an optionally at least mono-substituted alkylene group and/or may be condensed with an

optionally at least mono-substituted mono- or polycyclic ring-system, or an  
optionally at least mono-substituted aryl- or heteroaryl radical, which may be  
bonded via an optionally at least mono-substituted alkylene group and/or may  
be condensed with an optionally at least mono-substituted mono- or polycyclic  
ring-system,

5

or R<sup>13b</sup> and R<sup>14b</sup> together with the bridging nitrogen atom form a saturated,  
unsaturated or aromatic heterocyclic ring, which may be at least mono-  
substituted and/or contain at least one further heteroatom as a ring member,

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R<sup>15b</sup> represents hydrogen, an unbranched or branched, saturated or  
unsaturated, optionally at least mono-substituted aliphatic radical, a saturated  
or unsaturated, optionally at least mono-substituted, optionally at least one  
heteroatom as ring member containing cycloaliphatic radical or an optionally at  
15       least mono-substituted aryl- or heteroaryl radical, which may be bonded via an  
optionally at least mono-substituted alkylene group and/or may be condensed  
with an optionally at least mono-substituted mono- or polycyclic ring-system,

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R<sup>16b</sup> represents an unbranched or branched, saturated or unsaturated,  
20       optionally at least mono-substituted aliphatic radical,

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R<sup>17b</sup> represents an unbranched or branched, saturated or unsaturated,  
optionally at least mono-substituted aliphatic radical, and

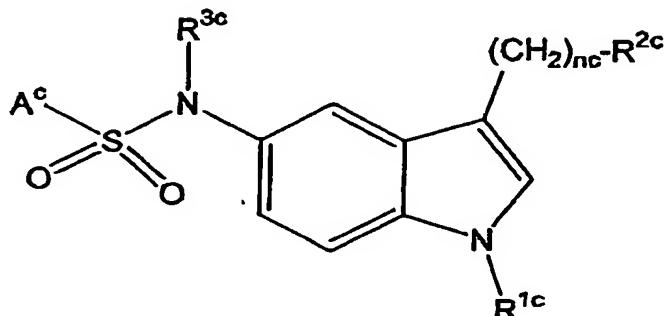
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R<sup>18b</sup> represents an optionally at least mono-substituted aryl radical

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optionally in form of one of its stereoisomers, preferably enantiomers or  
diastereomers, its racemate or in form of a mixture of at least two of its  
stereoisomers, preferably enantiomers or diastereomers, in any mixing ratio,  
or a physiologically acceptable salt thereof, or a solvate, respectively, and

compounds derived from sulfonamide of general formula (Ic),



(Ic)

wherein

- 10       $R^{1c}$  represents hydrogen, an optionally at least mono-substituted, linear or branched alkyl radical, an optionally at least mono-substituted phenyl radical or an optionally at least mono-substituted benzyl radical,
- 15       $R^{2c}$  represents a  $-NR^{4c}R^{5c}$  moiety or a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing cycloaliphatic radical, which may be condensed with a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing mono- or bicyclic cycloaliphatic ringsystem,
- 20       $R^{3c}$  represents hydrogen or an optionally at least mono- substituted, linear or branched alkyl radical,
- 25       $R^{4c}$  and  $R^{5c}$ , identical or different, represent hydrogen or an optionally at least mono-substituted, linear or branched alkyl radical, or

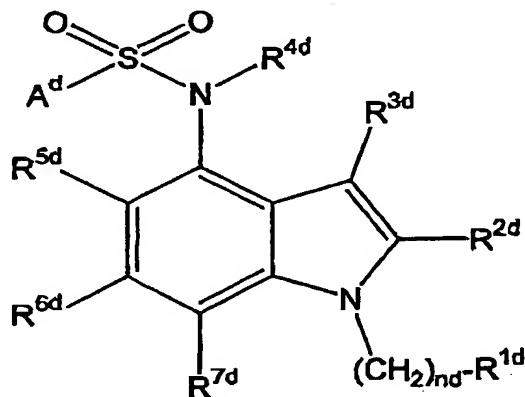
5       $R^{4c}$  and  $R^{5c}$  together with the bridging nitrogen atom form an optionally at least mono-substituted, saturated or unsaturated heterocyclic ring, which may contain at least one further heteroatom as a ring member and/or may be condensed with a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing mono- or bicyclic cycloaliphatic ringsystem,

10      $A^c$  represents an optionally at least mono-substituted mono- or polycyclic aromatic ringsystem, which may be bonded via an optionally at least mono-substituted alkylene-, an optionally at least mono-substituted alkenylene- or an optionally at least mono-substituted alkynylene group and/or may contain at least one heteroatom as a ring member in one or more of its rings.

15      $n_c$  represents 0, 1, 2, 3 or 4;

20     optionally in form of one of its stereoisomers, preferably enantiomers or diastereomers, its racemate or in form of a mixture of at least two of its stereoisomers, preferably enantiomers or diastereomers, in any mixing ratio, or a corresponding physiologically acceptable salt or a corresponding solvate,

and compounds of general formula (Id)



(Id)

5      R<sup>1d</sup> represents a -NR<sup>8d</sup>R<sup>9d</sup> radical or a saturated or unsaturated, optionally at least mono-substituted cycloaliphatic radical, which may contain at least one heteroatom as a ring member and/or which may be condensed with a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as a ring member containing mono- or bicyclic cycloaliphatic ring system,

10     R<sup>2d</sup>, R<sup>3d</sup>, R<sup>5d</sup>, R<sup>6d</sup> and R<sup>7d</sup>, identical or different, each represent hydrogen, halogen, nitro, alkoxy, cyano, a saturated or unsaturated, linear or branched, optionally at least mono-substituted aliphatic radical, or an optionally at least mono-substituted phenyl or an optionally at least mono-substituted heteroaryl radical,

15     R<sup>4d</sup> is hydrogen or a saturated or unsaturated, linear or branched, optionally at least mono-substituted aliphatic radical,

20     R<sup>8d</sup> and R<sup>9d</sup>, identical or different, each represent hydrogen or a saturated or unsaturated, linear or branched, optionally at least mono-substituted aliphatic radical,

or

25     R<sup>8d</sup> and R<sup>9d</sup> together with bridging nitrogen atom form a saturated or unsaturated, optionally at least mono-substituted heterocyclic ring, which may contain at least one additional heteroatom as a ring member and/or may be condensed with a saturated or unsaturated, optionally at least mono-substituted mono- or bicyclic cycloaliphatic ring system, which may optionally contain at least one heteroatom as a ring member,

30     A<sup>d</sup> represents an optionally at least mono-substituted mono- or polycyclic aromatic ring system, which may be bonded via an optionally at least mono-substituted alkylene, alkenylene or alkynylene group and/or which may contain at least one heteroatom as a ring member in one or more of its rings,

and

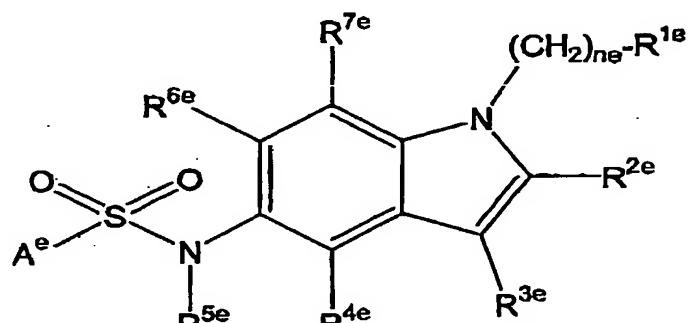
nd is 0, 1, 2, 3 or 4;

5

optionally in form of one of its stereoisomers, preferably enantiomers or diastereomers, its racemate or in form of a mixture of at least two of its stereoisomers, preferably enantiomers or diastereomers, in any mixing ratio, or a salt thereof, preferably a corresponding, physiologically acceptable salt thereof, or a corresponding solvate thereof.

10

and compounds derived from sulfonamide of general formula (Ie)



15

(Ie)

wherein

20

R<sup>1e</sup> represents an -NR<sup>8e</sup>R<sup>9e</sup> radical or a saturated or unsaturated, optionally at least mono-substituted cycloaliphatic radical, which may optionally contain at least one heteroatom as a ring member and/or which may be condensed with a saturated or unsaturated, optionally at least mono-substituted mono- or bicyclic cycloaliphatic ring system, which may optionally contain at least one heteroatom as a ring member,

25

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GENERIC

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5       $R^{2e}$ ,  $R^{3e}$ ,  $R^{4e}$ ,  $R^{6e}$  and  $R^{7e}$ , identical or different, each represent hydrogen, halogen, nitro, alkoxy, cyano, a saturated or unsaturated, linear or branched, optionally at least mono-substituted aliphatic radical or an optionally at least mono-substituted phenyl radical or an optionally at least mono-substituted heteroaryl radical,

10      $R^{5e}$  represents hydrogen or a saturated or unsaturated, linear or branched, optionally at least mono-substituted aliphatic radical,

15      $R^{8e}$  and  $R^{9e}$ , identical or different, each represent hydrogen or a saturated or unsaturated, linear or branched, optionally at least mono-substituted aliphatic radical,

or

20      $R^{8e}$  and  $R^{9e}$  together with the bridging nitrogen atom form a saturated or unsaturated, optionally at least mono-substituted heterocyclic ring, which may contain at least one additional heteroatom as a ring member and/or which may be condensed with a saturated or unsaturated, optionally at least mono-substituted, mono- or bicyclic cycloaliphatic ring system which may optionally contain at least one heteroatom as a ring member,

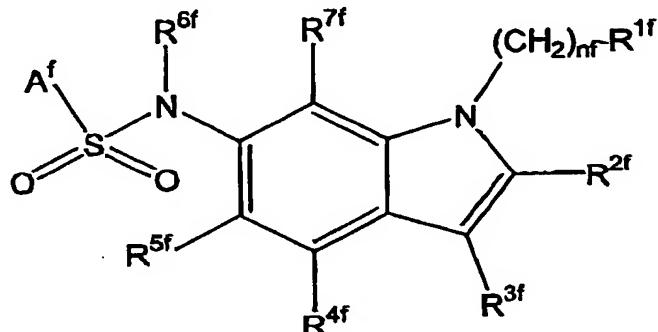
25      $A^e$  represents an optionally at least mono-substituted mono- or polycyclic aromatic ring system, which may be bonded via an optionally at least mono-substituted alkylene, alkenylene or alkynylene group and/or which may contain at least one heteroatom as a ring member in one or more of its rings,

and

30      $n_e$  is 0, 1, 2, 3 or 4;

optionally in the form of one of its stereoisomers, preferably enantiomers or diastereomers, its racemate or in the form of a mixture of at least two of its stereoisomers, preferably enantiomers or diastereomers, at any mixture ratio, or a corresponding, physiologically acceptable salt, or a corresponding solvate, and compounds derived from sulfonamide of general formula (If)

5



(If)

wherein

10

$R^{1f}$  represents a  $-NR^{8f}R^{9f}$  radical or a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as a ring member containing cycloaliphatic radical, which may be condensed with a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as a ring member containing mono- or bicyclic cycloaliphatic ring system,

15

20

$R^{2f}$ ,  $R^{3f}$ ,  $R^{4f}$ ,  $R^{5f}$  and  $R^{7f}$ , identical or different, each represent hydrogen, halogen, nitro, alkoxy, cyano, a saturated or unsaturated, linear or branched, optionally at least mono-substituted aliphatic radical, or an optionally at least mono-substituted phenyl radical or an optionally at least mono-substituted heteroaryl radical,

25

$R^{6f}$  represents hydrogen or a saturated or unsaturated, linear or branched, optionally at least mono-substituted aliphatic radical,

R<sup>8f</sup> and R<sup>9f</sup>, identical or different, each represent hydrogen or a saturated or unsaturated, linear or branched, optionally at least mono-substituted aliphatic radical,

5 or

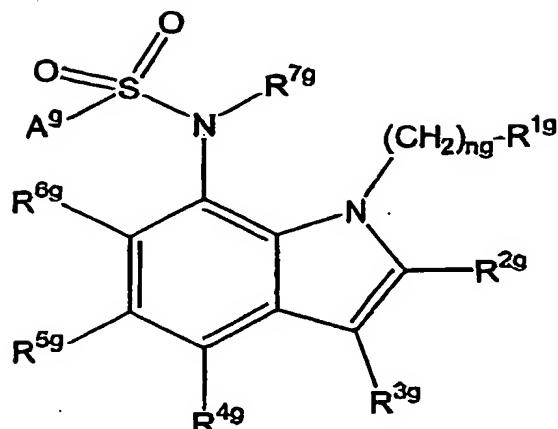
10 R<sup>8f</sup> and R<sup>9f</sup>, together with the bridging nitrogen atom, form a saturated or unsaturated, optionally at least mono-substituted heterocyclic ring, which may contain at least one further heteroatom as a ring member and/or which may be condensed with a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as a ring member containing mono- or bicyclic cycloaliphatic ring system,

15 A<sup>f</sup> represents an optionally at least mono-substituted mono- or polycyclic aromatic ring system, which may be bonded via an optionally at least mono-substituted alkylene, alkenylene or alkynylene group and/or which may contain at least one heteroatom as a ring member in one or more of its rings

and

20 n<sub>f</sub> is 0, 1, 2, 3 or 4;

25 optionally in the form of one of its stereoisomers, preferably enantiomers or diastereomers, its racemate or in the form of a mixture of at least two of its stereoisomers, preferably enantiomers or diastereomers, at any mixture ratio, or a corresponding, physiologically acceptable salt, or a corresponding solvate, and compounds derived from sulfonamide of general formula (Ig)



wherein

5

$R^{1g}$  is a  $-NR^{8g}R^{9g}$  radical or a saturated or unsaturated, optionally at least mono-substituted cycloaliphatic radical, which may optionally contain at least one heteroatom as a ring member and which may be condensed with a saturated or unsaturated, optionally at least mono-substituted mono- or bicyclic cycloaliphatic ring system which may optionally contain at least one heteroatom as a ring member,

10

$R^{2g}$ ,  $R^{3g}$ ,  $R^{4g}$ ,  $R^{5g}$  and  $R^{6g}$ , identical or different, each represent hydrogen, halogen, nitro, alkoxy, cyano, a saturated or unsaturated, linear or branched, optionally at least mono-substituted aliphatic radical, or an optionally at least mono-substituted phenyl radical or an optionally at least mono-substituted heteroaryl radical,

15

$R^{7g}$  represents hydrogen or a saturated or unsaturated, linear or branched, optionally at least mono-substituted aliphatic radical,

20

$R^{8g}$  and  $R^{9g}$ , identical or different, represent hydrogen or a saturated or unsaturated, linear or branched, optionally at least mono-substituted aliphatic radical,

25

or

5

$R^{8g}$  and  $R^{9g}$  together with the bridging nitrogen atom form a saturated or unsaturated, optionally at least mono-substituted heterocyclic ring, which may contain at least one additional heteroatom as a ring member and/or which may be condensed with a saturated or unsaturated, optionally at least mono-substituted mono- or bicyclic cycloaliphatic ring system, which may optionally contain at least one heteroatom as a ring member,

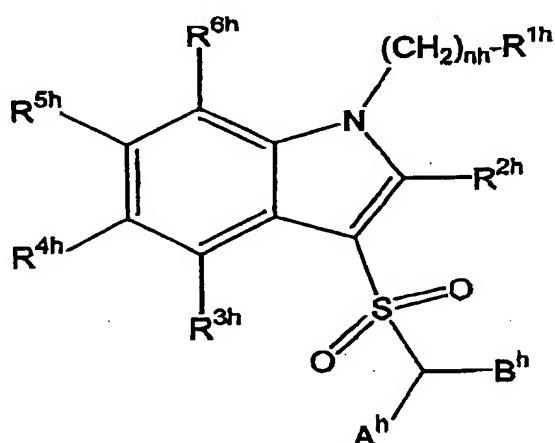
10

$A^g$  represents an optionally at least mono-substituted mono- or polycyclic aromatic ring system, which may be bonded via an optionally at least mono-substituted alkylene, alkenylene or alkynylene group and/or which may contain at least one heteroatom as a ring member in one or more of its rings.

ng is 0, 1, 2, 3 or 4;

15

optionally in the form of one of its stereoisomers, preferably enantiomers or diastereomers, its racemate or in the form of a mixture of at least two of its stereoisomers, preferably enantiomers or diastereomers, at any mixture ratio, or a corresponding, physiologically acceptable salt, or a corresponding solvate and compounds derived from sulfonamide of general formula (Ih)



(Ih)

wherein

25

5       $R^{1h}$  represents a  $-NR^{7h}R^{8h}$  radical or a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as a ring member containing cycloaliphatic radical, which may be condensed with a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as a ring member containing mono- or bicyclic cycloaliphatic ring system,

10      $R^{2h}$ ,  $R^{3h}$ ,  $R^{4h}$ ,  $R^{5h}$  and  $R^{6h}$ , identical or different, each represent hydrogen, halogen, cyano, nitro, a linear or branched alkyl radical, a linear or branched alkenyl radical, a linear or branched alkinyl radical, a linear or branched alkoxy radical, a linear or branched alkylthio radical, hydroxy, trifluoromethyl, a cycloalkyl radical, a cycloalkenyl radical, an alkylcarbonyl radical, a phenylcarbonyl or a  $-NR^{9h}R^{10h}$  group,

15      $R^{7h}$  and  $R^{8h}$ , identical or different, each represent hydrogen or a saturated or unsaturated, optionally at least mono-substituted linear or branched aliphatic radical,

20     or

25      $R^{7h}$  and  $R^{8h}$ , together with the bridging nitrogen atom form a saturated or unsaturated, optionally at least mono-substituted, optionally at least one further heteroatom as a ring member containing heterocyclic ring which may be condensed with a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as a ring member containing mono- or bicyclic cycloaliphatic ring system.

30      $R^{9h}$  and  $R^{10h}$ , identical or different, each represent hydrogen or a saturated or unsaturated, linear or branched, optionally at least mono-substituted aliphatic radical,

35     or

R<sup>9n</sup> and R<sup>10n</sup>, together with the bridging nitrogen atom form a saturated or unsaturated, optionally at least mono-substituted, optionally at least one further heteroatom as a ring member containing heterocyclic ring which may be condensed with a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as a ring member containing mono- or bicyclic cycloaliphatic ring system.

5

A<sup>h</sup> and B<sup>h</sup>, identical or different, each represent a saturated or unsaturated, linear or branched, optionally at least mono-substituted aliphatic radical

10

or

15

A<sup>h</sup> and B<sup>h</sup>, together with the carbon atom to which they are bonded, form a saturated or unsaturated, but not aromatic, optionally at least mono-substituted cycloalkyl ring,

and

nh is 0, 1, 2, 3 or 4

20

optionally in the form of one of their stereoisomers, preferably enantiomers or diastereomers, their racemate or in the form of a mixture of at least two of their stereoisomers, preferably enantiomers or diastereomers, at any mixture ratio, or a corresponding physiologically acceptable salt or a corresponding solvate.

25

2. The combination according to claim 1, characterized in that it comprises 1-99% by weight of component (A) and 99-1% by weight of component (B), more preferably 10-80% by weight of component (A) and 90-20% by weight of component (B), in each case referring to the total weight of both components (A) and (B).

3. A medicament comprising an active substance combination according to claim 1 or 2 and optionally one or more pharmacologically acceptable adjuvants.
4. A medicament according to claim 3 for regulation of appetite, for maintenance, increase or reduction of body weight, for prophylaxis and/or treatment of disorders related to food ingestion, preferably for prophylaxis and/or treatment of obesity, anorexia, cachexia, bulimia, diabetes, preferably type II diabetes (non-insulin-dependent diabetes mellitus), or for prophylaxis and/or treatment of gastrointestinal tract disorders, preferably of the irritable bowel syndrome, for prophylaxis and/or treatment of Peripheral Nervous System Disorders, Central Nervous System Disorders, arthritis, epilepsy, anxiety, panic, depression, cognitive disorders, memory disorders, cardiovascular diseases, 10 senile dementia processes, such as Alzheimer's, Parkinson's and/or Huntington's Disease, schizophrenia, psychosis, infantile hyperkinesia (ADHD, attention deficit / hyperactivity disorder), pain, hypertensive syndrome, inflammatory diseases, immunologic diseases or for improvement of cognition.
- 15 5. Use of the combination according to claim 1 or 2 for the manufacture of a medicament for regulation of appetite.
- 20 6. Use of the combination according to claim 1 or 2 for the manufacture of a medicament for maintenance, increase or reduction of body weight.
- 25 7. Use of the combination according to claim 1 or 2 for the manufacture of a medicament for prophylaxis and/or treatment of disorders related to food ingestion, preferably for prophylaxis and/or treatment of obesity, anorexia, cachexia, bulimia, diabetes, preferably type II diabetes (non-insulin-dependent diabetes mellitus).
- 30 8. Use of the combination according to claim 1 or 2 for the manufacture of a medicament for prophylaxis and/or treatment of gastrointestinal tract disorders, preferably of the irritable bowel syndrome.

9. Use of the combination according to claim 1 or 2 for the manufacture of a medicament for prophylaxis and/or treatment of Peripheral Nervous System Disorders.
- 5 10. Use of the combination according to claim 1 or 2, for the manufacture of a medicament for prophylaxis and/or treatment of Central Nervous System Disorders.
- 10 11. Use of the combination according to claim 1 or 2 for the manufacture of a medicament for prophylaxis and/or treatment arthritis.
12. Use of the combination according to claim 1 or 2 for the manufacture of a medicament for prophylaxis and/or treatment of epilepsy.
- 15 13. Use of the combination according to claim 1 or 2 for the manufacture of a medicament for prophylaxis and/or treatment of anxiety.
14. Use of the combination according to claim 1 or 2 for the manufacture of a medicament for prophylaxis and/or treatment of panic.
- 20 15. Use of the combination according to claim 1 or 2 for the manufacture of a medicament for prophylaxis and/or treatment of depression.
16. Use of the combination according to claim 1 or 2 for the manufacture of a medicament for prophylaxis and/or treatment of bipolar disorders.
- 25 17. Use of the combination according to claim 1 or 2 for the manufacture of a medicament for prophylaxis and/or treatment of cognitive disorders.
- 30 18. Use of the combination according to claim 1 or 2 for the manufacture of a medicament for prophylaxis and/or treatment of memory disorders.
19. Use of the combination according to claim 1 or 2 for the manufacture of a medicament for prophylaxis and/or treatment of cardiovascular diseases.

20. Use of the combination according to claim 1 or 2 for the manufacture of a medicament for prophylaxis and/or treatment of senile dementia processes.
- 5 21. Use of the combination according to claim 1 or 2 for the manufacture of a medicament for prophylaxis and/or treatment of neurodegenerative disorders, preferably Alzheimer's disease, Parkinson's disease, Huntington's disease and/or multiple sclerosis.
- 10 22. Use of the combination according to claim 1 or 2 for the manufacture of a medicament for prophylaxis and/or treatment of schizophrenia.
23. The use of the combination according to claim 1 or 2 for the manufacture of a medicament for prophylaxis and/or treatment of psychosis.
- 15 24. Use of the combination according to claim 1 or 2 for the manufacture of a medicament for prophylaxis and/or treatment of infantile hyperkinesia (ADHD, attention deficit / hyperactivity disorder).
- 20 25. The use of the combination according to claim 1 or 2 for the manufacture of a medicament for prophylaxis and/or treatment of pain.
26. Use of the combination according to claim 1 or 2 for the manufacture of a medicament for prophylaxis and/or treatment of hypertensive syndrome.
- 25 27. Use of the combination according to claim 1 or 2 for the manufacture of a medicament for prophylaxis and/or treatment of inflammatory diseases.
- 30 28. Use of the combination according to claim 1 or 2 for the manufacture of a medicament for prophylaxis and/or treatment of immunologic diseases.
29. The use of the combination according to claim 1 or 2 for the manufacture of a medicament for improvement of cognition.

30. A pharmaceutical formulation, characterized in that it comprises an active substance combination according to claim 1 or 2 and optionally one or more pharmacologically acceptable adjuvants.
- 5 31. The pharmaceutical formulation according to claim 30, characterized in that it is present in solid pharmaceutical forms such as tablets, tablets, chewing tablets, chewing gums, dragées, capsules, suppositories, powder preparations, transdermal therapeutic systems, transmucosal therapeutic systems, or in liquid and semi-liquid pharmaceutical forms such as drops or such as juice, sirup, solution, emulsion, suspension, preferably in form of tablets, capsules, drops or solution.
- 10
32. The pharmaceutical formulation according to claim 30, characterized in that it is present in form of multiple particles, preferably microtablets, microcapsules, microspheroids, granules, crystals or pellets, optionally compacted in a tablet, filled in a capsule or suspended in a suitable liquid.
- 15
33. The pharmaceutical formulation according to one or more of claims 30-32, characterized in that it is for oral, intravenous, intramuscular, subcutaneous, intrathecal, epidural, buccal, sublingual, pulmonal, rectal, transdermal, nasal or 20 intracerebroventricular application, preferably oral or intravenous.
34. The pharmaceutical formulation according to one or more of claims 30-32, characterized in that at least one of the components of the active substance combination (A) or (B) is present at least partially in sustained-release form.
- 25
35. The pharmaceutical formulation according to claim 34, characterized in that the medicament has at least one coating or at least one matrix comprising at least one material, which sustains active substance release.

36. The pharmaceutical formulation according to claim 35, characterized in that the sustained-release material is based on optionally modified, water-insoluble, natural, semisynthetic or synthetic polymer, or a natural wax or fat or fatty alcohol or semisynthetic or synthetic fatty acid, or on a mixture of at least 5 two of these afore mentioned components.
37. The pharmaceutical formulation according to claim 36, characterized in that the water-insoluble polymer is based on an acrylic resin, which is preferably selected from the group of poly(meth)acrylates, poly(C<sub>1-4</sub>)dialkylamino(C<sub>1-4</sub>)alkyl (meth)acrylates and/or copolymers thereof or a mixture of at least two 10 of the afore-mentioned polymers.
38. The pharmaceutical formulation according to claim 36, characterized in that the water-insoluble polymers are cellulose derivatives, preferably alkyl cellulose and even more preferably ethyl cellulose, or cellulose esters. 15
39. The pharmaceutical formulation according to claim 36, characterized in that the wax is carnauba wax, beeswax, glycerol monostearate, glycerol monobehenate, glycerol ditripalmitostearate, microcrystalline wax or a mixture 20 of at least two of these components.
40. The pharmaceutical formulation according to one or more of claims 36 to 39, characterized in that polymers have been used in combination with one or more plasticizers. 25
41. The pharmaceutical formulation according to one or more of claims 34 to 40, characterized in that besides the sustained-release form, at least one of the active substance components (A) or (B) is present in a non-sustained-release form. 30